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EXAMINER	
DAVIS, MINH TAM B	
ART UNIT	**PAPER NUMBER**
1642	7

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Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Applicati n N . 09/824,134	Applicant(s) WALLACH ET AL.
	Examiner MINH-TAM DAVIS	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-7 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's election of group I, claims 1-7, 11 in paper No: 6 is acknowledged. Accordingly, claims 1-7, 11 are examined in the instant application.

PRIORITY DATE

The Examiner has established a priority date 12/14/1995 for the instantly claimed application serial number 09/824134 as the foreign applications ISREAL 112022, ISREAL 112692 and ISREAL 114615 to which priority is claimed are not available in certified and translated copies. Applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

Claim Rejections - 35 USC § 112, SECOND PARAGRAPH

Claims 1-7, 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims 1-7, 11 are indefinite for the use of the language "moderately stringent conditions" in claims 1 and 11. Moderately stringent conditions are not defined by the claim (which reads on the full range of moderately stringent conditions), the specification does not provide a standard for ascertaining the requisite degree of moderately stringent conditions and one of ordinary skill in the art would not be

reasonably apprised of the scope of the invention and would not be able to determine the metes and bounds of the claims.

2. Claim 11 is indefinite, because claim 11 is dependent on non-elected claim 8.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims 1, item 2, and claims 2-7, 11 are rejected under 112, first paragraph.

The claim 1, item 2, and claims 2-7 are drawn to a DNA sequence that encodes an analog of MORT-1 protein of SEQ ID NO:2, which binds with the intracellular domain of the FAS ligand receptor (FAS-IC), which DNA sequence is capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions. The claims are further drawn to vectors comprising the above sequence, host cells transfected with said sequence and a method producing a polypeptide which binds with the intracellular domain of the FAS ligand receptor.

Claim 11 is drawn to a pharmaceutical composition comprising a recombinant animal virus vector encoding a protein capable of binding a cell surface receptor, and encoding a polypeptide "comprising" the Mort-1 protein of SEQ ID NO:2, or an analog of the MORT-1 protein of SEQ ID NO:2, which binds with the intracellular domain of the FAS ligand receptor, which DNA sequence is capable of hybridization with the cDNA

encoding SEQ ID NO:2 under moderately stringent conditions, or a fragment of said Mort-1 protein which binds with FAS-IC.

The specification discloses isolation of the claimed polynucleotide sequence, which encodes a MORT-1 protein or SEQ ID NO:2. The specification further discloses that only via it's own "death domain" comprising the amino acid sequence of residues 153 to 215, MORT-1 can bind to the FAS ligand receptor, via the "death domain" of the FAS ligand receptor, which is located within the intracellular domain of the FAS ligand receptor (page 36 and table 1 on page 37). The specification discloses that transfection of cells with HF-1, which is the same as the claimed polynucleotide sequence, which encodes a MORT-1 protein or SEQ ID NO:2, as well as p55-IC and FAS-IC, results in significant cell death, greater than that caused by FAS-IC expression (page 42, 4th paragraph, and figure 6). The specification however also discloses that high expression of p55-IC alone triggers a cytocidal effect, and that the expression of Fas-IC in Hela cells also have such an effect, although to a lower extent (page 42, 4th paragraph).

It is noted that it is not clear whether cell death is due to the activation of FAS ligand receptor by MORT-1 protein or due to the expression of p55-IC in the above transfected cells. In other words, binding to the FAS ligand receptor, via the "death domain" of the FAS ligand receptor, which is located within the intracellular domain of the FAS ligand receptor, is only a physical property and not a function of the Mort-1 protein encoded by the claimed polynucleotide, because it has not been shown that binding alone by the MORT-1 protein to the FAS ligand receptor is sufficient for the activation of FAS ligand receptor.

The claims, as written, however, encompass unrelated polynucleotides which share with the polynucleotide sequence encoding SEQ ID NO:2 a polynucleotide fragment encoding the "death domain" or the amino acid fragments of residues 153-215 of SEQ ID NO:2, and a viral vector comprising said unrelated polynucleotides.

The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural freatures common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive strutural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed and no identifying characteristic or property of the instant

polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific nucleotide sequences and the ability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed. Thus, only isolated DNA molecules encoding SEQ ID NO: 2, but not the full breadth of the claims meet the written description provisions of 35 USC 112, first paragraph.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 11 is drawn to a pharmaceutical composition for modulating the FAS-R ligand effect on cells comprising a recombinant animal virus vector encoding a protein capable of binding a cell surface receptor, and Mort-1 protein of SEQ ID NO:2.

Inherent in a "pharmaceutical composition' is *in vivo* use thereof.

The specification discloses isolation of the claimed polynucleotide sequence, which encodes a MORT-1 protein or SEQ ID NO:2. The specification further discloses

that only via it's own "death domain" in the amino acid sequence of residues130-245, MORT-1 can bind to the FAS ligand receptor, via the "death domain" of the FAS ligand receptor, which is located within the intracellular domain of the FAS ligand receptor (page 36 and table 1 on page 37). The specification discloses that transfection of cells with HF-1, which is the same as the claimed polynucleotide sequence, which encodes a MORT-1 protein or SEQ ID NO:2, as well as p55-IC and FAS-IC, results in significant cell death, greater than that caused by FAS-IC expression (page 42, 4th paragraph, and figure 6). The specification however also discloses that high expression of p55-IC alone triggers a cytocidal effect, and that the expression of Fas-IC in Hela cells also have suchan effect, although to a lower extent (page 42, 4th paragraph).

The specification further discloses that it is well known in the art that FAS receptor (FAS-R) mediates cell death in the form of apoptosis (p.3, second paragraph). The specification contemplates the use of the polynucleotide encoding SEQ ID NO:2 to mimic or enhance the function of FAS-R ligand, for application such as anti-tumor, anti-inflammatory or anti-HIV application (p.17).

The claim 11 encompasses a composition comprising recombinant animal virus vector encoding a protein capable of binding a cell surface receptor, and said Mort-1 protein for gene therapy for treating tumors or inflammation or HIV.

It is noted that it is not clear whether cell death is due to the activation of FAS ligand receptor by MORT-1 protein or due to the expression of p55-IC in the above transfected cells. In other words, it has not been shown that binding alone by the

MORT-1 protein to the FAS ligand receptor is sufficient for the activation of FAS ligand receptor, which in turn causes cell death.

Further, even if the MORT-1 protein binds and activates FAS receptor in transfected cells, resulting in cell death, one cannot extrapolate the *in vitro* transfection conditions with *in vivo* conditions, because usually in *in vitro* transfection, the proteins introduced into the cells are overexpressed in an artificially over-abundant amount, thus increasing the chance of interaction between the introduced proteins which otherwise might not happen *in vivo,* and because *in vitro* conditions cannot duplicate the complex *in vivo* conditions. Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teach that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived.

Moreover, it is well known in the art that gene therapy is unpredictable. The state of the art at the time of filing was that the combination of vector, promoter, protein, cell, target tissue, level of expression and route of administration required to target the tissue of interest and obtain a therapeutic effect using gene therapy was unpredictable. For example, Miller (1995, FASEB J., Vol. 9, pages 190-199) review the types of vectors

available for *in vivo* gene therapy, and conclude that "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances...targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (page 198, column 1). Deonarain (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicate that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art which show promise but states that such techniques are even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section). Verma (Sept. 1997, Nature, Vol. 389, pages 239-242) reviews vectors known in the art for use in gene therapy and discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (see entire article). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (page 240, sentence bridging columns 2 and 3). Crystal (1995, Science, Vol. 270, page 404-410) also reviews various vectors known in the art and indicates that "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409).

In addition, one cannot extrapolate the teaching of the specification to the claims because it is well known that the art of anticancer drug discovery for cancer therapy is highly unpredictable. Such unpredictability would apply as well to treatment of inflammation and HIV. Gura (Science, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second para). Because of the known unpredictability of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the claimed recombinant viral vector could be effectively used for treating cancer or inflammation or HIV. Further, the refractory nature of cancer to drugs is well known in the art. Jain (Sci. Am., 1994, 271:58-65) teaches that tumors resist penetration by drugs (p.58, col 1) and that scientists need to put expanded effort into uncovering the reasons why therapeutic agents that show encouraging promise in the laboratory often turn out to be ineffective in the treatment of common solid tumors (p. 65, col 3). Curti (Crit. Rev. in Oncology/Hematology, 1993, 14:29-39) teaches that solid tumors resist destruction by chemotherapy agents and that although strategies to overcome defense mechanisms of neoplastic cells have been developed and tested in a number of patients, success has been limited and further teaches that it is certainly possible that cancer cells possess many as yet undefined additional molecular mechanisms to defeat chemotherapy treatment strategies and if this is true, designing effective

chemotherapeutic regimens for solid tumors may prove a daunting task (para bridging pages 29-30) and concludes that knowledge about the physical barriers to drug delivery in tumors is a work in progress (p. 36, col 2). It is clear that based on the state of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the claimed recombinant viral vector could be effectively used for treating cancer or inflammation or HIV. In addition, Hartwell et al (Science, 1997, 278:1064-1068) teach that an effective chemotherapeutic must selectively kill tumor cells, that most anticancer drugs have been discovered by serendipity and that the molecular alterations that provide selective tumor cell killing are unknown and that even understanding the detailed molecular mechanism by which a drug acts often provides little insight into why the treated tumor cell dies (para bridging pages 1064-1065) and Jain (cited supra) specifically teaches that systemic treatment typically consists of chemotherapeutic drugs that are toxic to dividing cells (p. 58, col 2, para 2).

Further, the claimed pharmaceutical composition must accomplish several tasks to be effective. It must be delivered into the circulation that supplies the target cells and interact at the proper site of action and must do so at a sufficient concentration and for a sufficient period of time. In addition the target cell must not have a alternate means of survival despite action at the proper site for the drug. *In vitro* assays cannot duplicate the complex conditions of *in vivo* therapy. In the assays, the claimed polynucleotides is transfected into cells and overexpressed during the entire assay period. This is not the case *in vivo*, where exposure to the target site may be delayed or inadequate. In addtion variables such as biological stability, half-life or clearance from the blood are

important parameters in achieving successful therapy. The encoded polypeptide may be inactivated *in vivo* before producing a sufficient effect, for example, by proteolytic degradation, immunological activation or due to an inherently short half life of the protein and the *in vitro* tests of record do not sufficiently duplicate the conditions which occur *in vivo*. In addition, the encoded polypeptide may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by fluids, cells and tissues where the encoded polypeptide has no effect, circulation into the target area may be insufficient to carry the encoded polypeptide and a large enough local concentration may not be established. Thus, based on the cell culture data presented in the specification, it could not be predicted that, in the *in vivo* environment, the claimed polynucleotide encoding Mort-1 protein or its analogs would be useful for treating cancer, inflammation and HIV.

In view of the above, it would have been undue experimentation to practice the claimed invention.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

If Applicant could overcome the above 112, first paragraph rejections, claim 11 is still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant animal virus vector encoding a protein capable of binding a target cell surface receptor, and Mort-1 protein of SEQ ID NO:2, does not reasonably provide enablement for a recombinant animal virus vector encoding a protein capable of binding any cell surface receptor, and Mort-1 protein of SEQ ID

NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 11 is drawn to a pharmaceutical composition for modulating the FAS-R ligand effect on cells comprising a recombinant animal virus vector encoding a protein capable of binding "a" cell surface receptor, and Mort-1 protein of SEQ ID NO:2.

Claim 11 encompasses a pharmaceutical composition for modulating the FAS-R ligand effect on cells comprising a recombinant animal virus vector encoding a protein capable of binding "any" cell surface receptor, and Mort-1 protein of SEQ ID NO:2.

It is not clear how one could use the claimed vector, because the complex of a cell surface receptor and Mort-1 protein would bind to any cell, and not necessarily to the target cells.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

1. Claim 1 (1) and (3) is rejected under 35 U.S.C. 102(a) as being anticipated by Boldin, MP et al, Genbank Sequence Database (Accession X84709), National Center for Biotechnology Information, National Library of Medicine, Bethesda, Maryland, publicly available on April 1995 and JBC, 1995, 270: 7795-7798.

Claim 1(1) is drawn to a DNA sequence which encodes the MORT-1 protein having the amino acid sequence of SEQ ID NO:2.

Claim 1(3) is drawn to a DNA coding sequence consisting of a DNA sequence which encodes a fragment of the MORT-1 protein which binds with FAS-IC.

The specification discloses that SEQ ID NO:1 encodes SEQ ID NO:2 (figure 4 legend, and sequence listing, on page 49).

Boldin et al teach a nucleic acid sequence which is 100% identical to SEQ ID NO:1 from nucleotide 1 to 1701, as shown in MPSRCH sequence similarity search (MPSRCH search report, 2002, us-09-824-134-1.rge, pages 1-2).

Boldin et al further teach the death domain (amino acids 130-245 in table 1) of the encoded MORT-1 protein, wherein via its death domain, MORT-1 binds to the intracellular domain of FAS (Fas-IC) (abstract).

Given the polynucleotide sequence taught by Boldin et al, one of ordinary skill in the art would immediately envision the claimed polynucleotides.

2. Claims 1 (2) and (3) and 2 are rejected under 35 U.S.C. 102(a) as being anticipated by Chinnaiyan, AM, et al, GenBank Database (Accession U24231 and Q13158), National Center for Biotechnology Information, National Library of Medicine, Bethesda, Maryland, publicly available on 1995, and Cell, 1995, 81: 505-512.

Claims 1 (2) and 2 are drawn to a DNA sequence encoding an analog of the MORT-1 protein of SEQ ID NO:2, which binds with the intracellular domain of the FAS ligand receptor, which DNA sequence is capable of hybridization with the cDNA encoding SEQ ID NO:2 under moderately stringent conditions. Claim 1(3) is drawn to a DNA coding sequence consisting of a DNA sequence which encodes a fragment of the MORT-1 protein which binds with FAS-IC.

The specification discloses that SEQ ID NO:1 encodes SEQ ID NO:2 (figure 4 legend). The specification further discloses that via it's own "death domain" comprising the amino acid sequence of residues 153 to 215, MORT-1 can bind to the FAS ligand receptor, via the "death domain" of the FAS ligand receptor, which is located within the intracellular domain of the FAS ligand receptor (page 36 and table 1 on page 37).

Chinnaiyan, AM, et al teach a nucleic acid sequence FADD, which is 99.8% similar to the claimed nucleic sequence of SEQ ID NO:1, encoding SEQ ID NO:2, from nucleotide 22 to nucleotide 1658, and the encoded amino acid sequence which is 99.5% similar to the claimed SEQ ID NO:2, from amino acid 49 to 256, wherein said protein contains a death domain and interacts with the death domain of FAS, as shown in MPSRCH sequence similarity search (MPSRCH search report, 2002, us-09-824-134-1.rge, pages 4-5, and MPSRCH search report, 2002, us-09-824-134-2.rpr, page 1).

Chinnaiyan, AM, et al further teach on figures 2 and 7 the encoded death domain, and the nucleic sequence encoding said death domain of FADD, wherein said death domain interacts with the death domain of FAS (p.507).

Thus the nucleic acid sequence encoding the amino acid sequence taught by Chinnaiyan, AM, et al comprises the claimed nucleic acid sequence encoding the amino acid sequence of residues 153 to 215 or the "death domain" of the claimed encoded SEQ ID NO:2, via which it binds to the "death domain" of the FAS ligand receptor.

The reference does not specifically teach a DNA sequence encoding an analog of the MORT-1 protein of SEQ ID NO:2, which binds with the intracellular domain of the FAS ligand receptor, which DNA sequence is capable of hybridization with the cDNA encoding SEQ ID NO:2 under moderately stringent conditions. However, the claimed nucleic acid sequence appears to be the same as the prior art nucleic acid sequence. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable diffrences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Further, the nucleic acid sequence encoding the death domain in figure 2 taught by Chinnaiyan, AM, et al seems to be the same as the claimed DNA coding sequence consisting of a DNA sequence which encodes a fragment of the MORT-1 protein which binds with FAS-IC.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1, items 1, 2, and 3 and claims 2-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boldin, MP et al, *supra*, and Chinnaiyan, AM, et al, *supra*, in view of US Patent No. 4,889,806 and Sambrook et al, 1989 (Molecular Cloning, A Laboratory Manual, 2nd Edition, Cold Spring Harbor Press, Cold Spring Harbor, p. 16.3-16.4).

The claim 1, items 1, 2, and 3 and claims 2-7 are drawn to 1) an expression vector containing a DNA sequence which encodes the MORT-1 protein having the amino acid sequence of SEQ ID NO:2, or a DNA sequence encoding an analog of the MORT-1 protein of SEQ ID NO:2, which binds with the intracellular domain of the FAS ligand receptor, which DNA sequence is capable of hybridization with the cDNA encoding SEQ ID NO:2 under moderately stringent conditions, or a DNA coding sequence consisting of a DNA sequence which encodes a fragment of the MORT-1 protein which binds with FAS-IC, 2) a host cell containing the vector and 3) a method for producing said polypeptide.

Boldin, MP et al and Chinnaiyan, AM, et al disclose as set forth above but differ from the instant invention in that they do not disclose 1) an expression vector containing a DNA sequence which encodes the MORT-1 protein having the amino acid sequence of SEQ ID NO:2, or a DNA sequence encoding an analog of the MORT-1 protein of

SEQ ID NO:2, which binds with the intracellular domain of the FAS ligand receptor, which DNA sequence is capable of hybridization with the cDNA encoding SEQ ID NO:2 under moderately stringent conditions, or a DNA coding sequence consisting of a DNA sequence which encodes a fragment of the MORT-1 protein which binds with FAS-IC , 2) a host cell containing the vector and 3) a method for producing said polypeptide.

US Patent No. 4,889,806 teach that with the advent of recombinant DNA and molecular cloning technology it is now conventional to transfer genetic information into plasmids or vectors constructed in vitro and then transferred into host cells and clonally propagated (col 1, lines 18-24).

Sambrook et al teach that cloned genes are conventionally expressed using expression vectors and that expression of cloned proteins have been used to: (1) confirm the identity of a cloned gene by using immunological or functional assays to detect the encoded protein; (2) produce large amounts of proteins of biological interest that are normally available in only limited quantities from natural sources; (3) to study the biosynthesis and intracellular transport of proteins following their expression in various cell types; and (4) to elucidate structure-function relationships by analyzing the properties of normal and mutant proteins (para bridging pages 16.3 and 16.4).

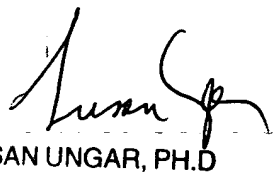
It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the polynucleotide of Boldin, MP et al or Chinnaiyan, AM, et al with the methods of Sambrook et al and US Patent No. 4,889,806 because US Patent No. 4,889,806 specifically teaches that it is conventional to transfer genetic materials into plasmids or vectors and then transfer the plasmids or vectors into

host cells and clonally propagate the genetic material and because Sambrook et al teach that cloned genes are conventionally expressed using expression vectors. One of ordinary skill in the art at the time the invention was made would have been motivated to combine the polynucleotide of Boldin, MP et al or Chinnaiyan, AM, et al with the methods of Sambrook et al and US Patent No. 4,889,806 because Sambrook et al specifically teach that expressed cloned proteins are used to: (1) confirm the identity of a cloned gene by using immunological or functional assays to detect the encoded protein; (2) produce large amounts of proteins of biological interest that are normally available in only limited quantities from natural sources; (3) to study the biosynthesis and intracellular transport of proteins following their expression in various cell types; and (4) to elucidate structure-function relationships by analyzing the properties of normal and mutant proteins. One of ordinary skill in the art would have been motivated to clone the claimed sequence in a vector, to transfect into a host cells, and to express it with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to clone the claimed sequence in a vector, to transfect into a host cells, and to express it to produce a large quantity of protein of biological interest, as taught by Sambrook et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.



SUSAN UNGAR, PH.D
PRIMARY EXAMINER

MINH TAM DAVIS

October 16, 2002